

Game changers: A new dawn for the treatment of cystic fibrosis

Doherty, P., & Downey, D. G. (2015). Game changers: A new dawn for the treatment of cystic fibrosis. *Ulster Medical Journal*, 84(3), 218-219. [http://www.ums.ac.uk/umj084/084\(3\)218.pdf](http://www.ums.ac.uk/umj084/084(3)218.pdf)

Published in:
Ulster Medical Journal

Document Version:
Publisher's PDF, also known as Version of record

Queen's University Belfast - Research Portal:
[Link to publication record in Queen's University Belfast Research Portal](#)

Publisher rights
© The Ulster Medical Society, 2015.
This work is made available online in accordance with the publisher's policies. Please refer to any applicable terms of use of the publisher.

General rights
Copyright for the publications made accessible via the Queen's University Belfast Research Portal is retained by the author(s) and / or other copyright owners and it is a condition of accessing these publications that users recognise and abide by the legal requirements associated with these rights.

Take down policy
The Research Portal is Queen's institutional repository that provides access to Queen's research output. Every effort has been made to ensure that content in the Research Portal does not infringe any person's rights, or applicable UK laws. If you discover content in the Research Portal that you believe breaches copyright or violates any law, please contact openaccess@qub.ac.uk.

Game Changers

TRANSANAL ENDOSCOPIC MICROSURGERY – CHANGING THE MANAGEMENT OF EARLY RECTAL CANCER

Mr Robert A. J. Spence, Ms Paula M. Loughlin, Mr Roger E. Lawther

Department of Surgery, Altnagelvin Hospital, Glenshane Road, BT47 6SB

Rectal cancer is the fifth most common cancer in adults. While the management of rectal cancer has become increasingly multimodal, surgical excision in the form of anterior resection, or abdomino-perineal excision, remains the primary intervention. There is debate about the optimum surgical approach to early stage rectal cancer (T1,N0), and endoscopically unresectable rectal polyps.

Transanal endoscopic microsurgery (TEM) has emerged as a less invasive alternative to traditional surgery. It is the intraluminal excision of a rectal lesion, with a clear, magnified view, using an operating rectoscope, allowing for organ-preserving surgery. TEM has a number of advantages over radical surgery, including avoidance of stoma, decreased pain, faster recovery, and much shorter hospital stay, typically 24 hours. Importantly, several studies comparing TEM to radical abdominal surgery show no significant difference in recurrence (4-8%), or survival. A recent meta-analysis comparing TEM with standard trans-anal surgery demonstrated a lower rate of margin involvement, decreased tumour recurrence, and reduced specimen fragmentation with TEM.

Careful patient selection is essential. TEM is now an accepted treatment for large benign polyps and early low risk rectal cancers (T1), which have no adverse pathological features. High-risk T1 tumours with poor differentiation and lymphatic involvement are better served with conventional resection. The use of TEM in node negative T2 and T3 tumours is unclear and requires further study. There is a role for TEM in the palliation of those with advanced rectal cancers, that due to co-morbidity, or metastatic disease, are unfit for major resection. As the use of this technique becomes more widespread, there are implications for service planning and training.

REFERENCES:

1. Kidane B, Chadi SA, Kanters S, et al. Local resection compared with radical resection in the treatment of T1N0M0 rectal adenocarcinoma: a systematic review and meta-analysis. *Dis Colon Rectum*. 2015 Jan;58(1):122-40.
2. Clancy C, Burke JP, Albert MR, et al. Transanal Endoscopic Microsurgery Versus Standard Transanal Excision for the Removal of Rectal Neoplasms: A Systematic Review and Meta-analysis. *Dis Colon Rectum*. 2015 Feb;58(2):254-61.

ENDOVASCULAR THERAPY FOR ACUTE ISCHAEMIC STROKE

Dr Paul A Burns.

Department of Radiology, Royal Victoria Hospital, Belfast, BT12 6BA

Stroke secondary to proximal vascular occlusion has a poor natural history unless rapid recanalization can be achieved. Unfortunately intravenous thrombolysis has modest efficacy at achieving this in the setting of a large clot burden¹. Endovascular therapy (mechanical thrombectomy) via utilizing a retrievable stent has shown promise to effect the rapid recanalization required.

The Royal Victoria Hospital, Belfast Trust was recently the sole UK recruiting centre for the ESCAPE trial¹, which compared outcome in anterior circulation stroke patients treated with endovascular therapy plus standard care versus standard care alone. Patients were selected into the study based on advanced CT imaging criteria, which had to demonstrate a small core infarct, proximal vascular occlusion and salvageable brain (that is ischemic, but not yet irreversibly infarcted). For patients randomized into the endovascular arm, emphasis was put on procedural speed, with a target CT to groin puncture of <60 minutes and groin puncture to procedure completion of <30 minutes.

The study demonstrated that the rate of functional independence at 90 days from stroke onset increased from 29.3% to 53.0% in the endovascular group and there was a decrease in mortality from 19.0% to 10.4%.

The American Heart Association/American Stroke Association in their updated guidelines has now endorsed endovascular therapy for selected stroke patients². As this therapy becomes standard of care, the challenge for us in Northern Ireland is to fully implement a 24/7 service and to ensure that patients eligible for this treatment are transferred as quickly as possible to benefit from it.

REFERENCES:

1. Goyal M, Demchuk AM, Menon BK, Eesa M, Rempel JL, Thornton J et al. Randomized assessment of rapid endovascular treatment of ischemic stroke. *NEJM*, 2015; 372:1019-1030
2. Powers WJ, Derdeyn CP, Biller J, Coffey CS, Hoh BL, Jauch EC et al; on behalf of the American Heart Association Stroke Council. 2015 AHA/ASA focused update of the 2013 guidelines for the early management of patients with acute ischemic stroke regarding endovascular treatment: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*, 2015; 46:000-000

A NEW DAWN FOR THE TREATMENT OF CYSTIC FIBROSIS

Dr Peter Doherty & Dr DG Downey

Belfast City Hospital, Belfast Health and Social Care Trust, Lisburn Rd, Belfast BT9 7AD

Cystic Fibrosis (CF) is an inherited, life limiting, multisystem disease characterized by viscid secretions in multiple organ systems. Progressive respiratory failure remains the most common cause of morbidity and mortality with a current median survival of 41 years. The disease affects over 10,000 people in the United Kingdom. The mainstay of therapy is the treatment and reduction of respiratory infections and optimizing nutritional status.

Cystic fibrosis is caused by a defect in the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) gene causing altered chloride and water transport. Over 2,000 different mutations of this gene have been described although not all cause CF. Approximately 50% of patients are homozygous for the $\Delta F508$ mutation.

Ivacaftor (Kalydeco) is the first in a new class of transformative medications known as CFTR Modulators. It improves the transport of chloride across the cell membrane resulting in a significant increase in lung function and a reduction in respiratory infections.¹ It is licensed for use in patients with the G551D and other similar mutations (5-10%

of patients).

More recently two positive phase III trials have been completed to assess the efficacy of Ivacaftor along with another CFTR Modulator, Lumacaftor, in patients homozygous for the $\Delta F508$ mutation.² This combination therapy (Orkambi) is currently licensed in the US with a European Medicine Agency review expected later in 2015. However, these drugs are expensive and the cost per quality adjusted life year (QALY) for Ivacaftor is between £285,000 and £1,077,000.³ There are several new CFTR modulators undergoing clinical trials at present.

REFERENCES:

1. Accurso FJ, Rowe SM, Clancy JP, Boyle MP, Dunitz JM, Durie PR et al. Effect of VX-770 in Persons with Cystic Fibrosis and the G551D-CFTR mutation. *N Engl J Med*. 2010 Nov 18; 363(21):1991-2003
2. Wainwright CE, Elborn JS, Ramsey BW, Marigowda G, Huang X, Cipolli M et al. Lumacaftor-Ivacaftor in Patients with Cystic Fibrosis Homozygous for Phe508del CFTR. *N Engl J Med*. 2015; 373:220-231
3. Cohen D, Raftery J. Paying twice: questions over high cost of cystic fibrosis drug developed with charitable funding. *BMJ*. 2014; 348:g1445